# METHOD FOR FABRICATING A HOLLOW MICRO-NEEDLE ARRAY

## Field of the Invention

0001 The present invention generally relates to a method for fabricating a hollow micro-needle array and the array fabricated. More particularly, the present invention relates to a method for fabricating a hollow micro-needle array wherein each of the micro-needles has a sharp end to facilitate penetration and the array fabricated.

## Background of the Invention

0002 Hollow micro-needle arrays have been used in medical technology for taking blood samples, for taking other fluid samples in minute quantities and for injection of medicine in biotechnology applications. Hollow micro-needle arrays which are fabricated of various types of materials, i.e., semiconductor materials, polymeric materials or metals have been utilized. When semiconductor materials are used for fabricating hollow micro-needle arrays, the arrays are mostly formed on silicon-based wafers or substrates. A conventional process utilizing semiconductor materials for fabricating hollow micro-needle arrays requires numerous steps of dry etching, wet etching and thin film

deposition. The fabrication process is complicated and time consuming. As a consequence, the yield of the process is poor and the fabrication cost is high.

0003 Hollow micro-needles fabricated by the conventional process usually have ends formed in spherical shape and thus are difficult for penetration during use. Moreover, the internal passageway in the micro-needle is normally larger at the root end of the needle compared to the tip end of the needle which limits the flow of fluid that passes through the micro-needle. In order to maintain the size of the internal passageway constant and the structural strength of the micro-needle, it is difficult to increase the array density for the micro-needles. As a result, the amount of the fluid sample taken by the micro-needles or the amount of fluid delivered by the micro-needles is frequently insufficient. The smaller internal passageway further increases the resistance to the fluid flow, thus requiring a larger driving force at the root end of the micro-needle which in turn increases the cost of the equipment that utilizes the micro-needle array.

0004 For conventional micro-needles that are equipped with spherical ends, i.e., without sharp points, the force required on the micro-needle for penetrating an organism is sufficiently high such that the needle must be constructed with sufficient strength by increasing its size in order to avoid the possibility of needle breakage during use.

0005 It is therefore an object of the present invention to provide a method for fabricating a hollow micro-needle array that does not have the drawbacks or shortcomings or the conventional methods.

0006 It is another object of the present invention to provide a hollow micro-needle array that can be fabricated by using semiconductor materials and processes.

0007 It is a further object of the present invention to provide a hollow micro-needle array that can be fabricated with reduced fabrication steps and at low cost.

## Summary of the Invention

0008 In accordance with the present invention, a method for fabricating a hollow micro-needle array and the hollow micro-needle array fabricated are disclosed.

0009 In a preferred embodiment, a method for fabricating a hollow micro-needle array can be carried out by the operating steps of providing a silicon substrate; depositing a protective layer on the silicon substrate; defining a plurality of regions for wet etching; wet etching the silicon substrate forming a plurality of recesses each having inclined sidewalls; and continuing processing the plurality of recesses forming a hollow micro-needle array.

00010 In the method for fabricating a hollow micro-needle array, the continuing processing step is selected from the group consisting of electroplating, imaging/developing and micro-machining. The method may further include the step of providing a polymeric substrate instead of the silicon substrate, and forming the plurality of recesses with inclined sidewalls by a laser processing technique. The method may further include the step of providing a photoresist material instead of the silicon substrate, and forming the plurality of recesses having inclined sidewalls by

imaging and developing. A tip portion of a micro-needle in the hollow micro-needle array is at least partially formed with an inclined plane. The continuing processing step may further include the sub-steps of photolithographically developing a photoresist material on top of the silicon substrate and forming a plurality of recesses; plating a metal in the plurality of recesses forming a plurality of metal micro-needles; removing the photoresist material exposing the plurality of hollow metal micro-needles; and etching the silicon substrate forming a plurality of hollow metal micro-needles. The method may further include the step of depositing a starting metal layer on the silicon substrate in the plurality of recesses that have inclined sidewalls.

00011 In the method, the plating step is selected from the group consisting of electroplating, electroless plating, evaporation and sputtering. The metal may be selected from the group consisting of copper, chromium, nickel, iron, gold, platinum, palladium, their alloys and stainless steel. The removal step for the photoresist material and the hollowing process for the micro-needles are carried out by a technique selected from the group consisting of laser processing, etching and photolithography. The method may further include the step of using the silicon substrate

with the metal micro-needles as a mold for fabricating a multiplicity of micro-needles. The multiplicity of micro-needles can further be fabricated by micro-injection molding or a micro-thermal compression forming technique.

00012 The present invention is further directed to a method for fabricating a hollow micro-needle array which can be carried out by the operating steps of providing a silicon substrate; depositing a protective layer on the silicon substrate; defining a plurality of wet etch regions; wet etching the plurality of wet etch regions on the silicon substrate forming a plurality of recesses, each having inclined sidewalls; depositing sequentially an anti-reflective coating layer and a sacrificial layer on top of the silicon substrate; depositing a photoresist layer; imaging the photoresist layer forming the micro-needle array; removing the sacrificial layer obtaining a bottom layer with inclined sidewalls; and developing the bottom layer forming a micro-needle array.

00013 The method for fabricating a hollow micro-needle array may further include the step, after the deposition of the photoresist layer, of removing the sacrificial layer and then imaging and developing the bottom structure. The sacrificial layer

may be a mold release layer. The method may further include the repeated steps of depositing the photoresist layer and imaging the photoresist layer such that an internal diameter of the flow passageway in the micro-needle array is changed for serving as a storage function.

00014 The present invention is still further directed to a method for fabricating a hollow micro-needle array which can be carried out by the operating steps of providing a silicon substrate; depositing a protective layer on top of the silicon substrate; defining a plurality of wet etching regions; wet etching the silicon substrate forming a plurality of recesses each having inclined sidewalls; depositing a sacrificial layer on top of the silicon substrate; compression molding by using a material having sufficient plasticity; removing the sacrificial layer; forming a bottom structure having inclined sidewalls and micro-machining the silicon substrate forming a micro-needle array.

00015 In the method for fabricating a hollow micro-needle array, the sacrificial layer may be a mold release layer. The material that has sufficient plasticity is selected from thermoplastic materials and thermosetting materials. The

compression molding step for the material with sufficient plasticity can be replaced by an injection molding process. The micro-processing step may include laser processing steps or etching steps.

## Brief Description of the Drawings

00016 These and other objects, features and advantages of the present invention will become apparent from the following detailed description and the appended drawings in which:

00017 Figures 1A-1H are enlarged, cross-sectional views illustrating the fabrication process steps for the present invention first preferred embodiment.

00018 Figures 2A-2F are enlarged, cross-sectional views illustrating the fabrication process steps for the present invention second preferred embodiment.

00019 Figures 3A-3C are enlarged, cross-sectional views illustrating the fabrication process steps for the present invention third preferred embodiment.

00020 Figures 4A-4H are enlarged, cross-sectional views illustrating the fabrication process steps for the present invention fourth preferred embodiment.

00021 Figures 5A-5G are enlarged, cross-sectional views illustrating the fabrication process steps for the present invention fifth preferred embodiment.

00022 Figure 6 are enlarged perspective and cross-sectional views illustrating the various recesses with inclined sidewalls and the shapes of the sharp points obtained for the micro-needles.

00023 Figure 7 are enlarged perspective and cross-sectional views illustrating the present invention recesses with inclined sidewalls and the sharp pointed micro-needles obtained.

00024 Figures 8A-8H are enlarged, cross-sectional views illustrating the fabrication process steps for the present invention sixth preferred embodiment.

Detailed Description of the Preferred and Alternate Embodiments

00025 The present invention discloses a method for fabricating a hollow micro-needle array with a simplified procedure at lower fabrication costs. In the method, micro-needles are fabricated each having an end with inclined surfaces, i.e. a sharp end. Since the sharp end of the micro-needles easily penetrates into an organism, the present invention hollow micro-needle array can be advantageously used in applications for drug dispensing and sampling.

00026 The present invention fabrication process for hollow micro-needle array can be started by a wet etch process carried out on a silicon wafer or a silicon substrate forming an indentation that has inclined sidewalls. The indentation is then used as a mold such a that micro-needle array can be produced by various technologies such as metal plating, imaging/developing and micro-processing.

00027 Referring initially to Figures 1A-1H, wherein enlarged, cross-sectional views illustrating fabrication process steps for the present invention first preferred embodiment for fabricating a hollow micro-needle array are shown. The process starts with a

silicon wafer 100 with its top surface 102, bottom surface 104 covered by a protective layer 110. The protective layer 110 can be advantageously formed of silicon nitride. This is shown in Figure 1A. In the next step of the process, shown in Figure 1B, a photoresist layer (not shown) is used to image and define an area 111 for a future wet etching process by etching away the protective layer 110. The wet etch area 111 is then wet etched to expose the silicon wafer 100, as shown in Figure 1C. Due to the an-isotropic nature of the wet etch process, a recess 101 that is formed with inclined sidewalls 106 is formed.

00028 A photolithographic method is then carried out on the bottom protective layer 110 to define areas 112 which will to be dry etched. As shown in Figure 1D, on top of the silicon wafer 100 is then performed a physical vapor deposition (or an evaporation method) to coat a metal layer 120 on top of the top protective layer 110. A suitable metal layer 120 can be deposited of a metal such as chromium, nickel or copper. A second photolithographic method is then carried out, as shown in Figure 1E, on top of the first metal layer 120 by first depositing a photoresist layer 130 on top of the first metal layer 120. In the photoresist layer 130, is then formed a plurality of plating areas 131 exposing partially

the first metal layer 120. The to be plated areas 131 are formed in a hollow micro-needle shape. This is shown in Figure 1E.

00029 In the next step of the process, the plating area 131 is filled with a plating metal on top of the first metal layer 120. A suitable plating metal may be copper or nickel. A metal micro-needle 140 is thus formed, as shown in Figure 1F. Since the metal atoms are arranged on the inclined surface 106 of the recess 101 during the plating process, the metal micro-needle 140 is formed with a sharp end shown in Figure 1F. In the final step of the process, as shown in Figure 1G, a demolding step is carried out by removing the photoresist material 130 such that the hollow metal micro-needle 140 is exposed. The silicon wafer 100 is then dry etched to form apertures 108 through the metal micro-needle 140.

00030 It should be noted that, in the above described process for forming the present invention first preferred embodiment micro-needle, the lithography process for defining the dry etch region 112 does not have to be carried out before the wet etch process, as long as it is carried out before the dry etch process. Furthermore, the plating technique for the metal can be advantageously selected from electroplating, electroless plating,

evaporation or sputtering. The deposition of the starting metal layer 120 is therefore not absolutely necessary. The metal material can be selected from nickel, iron, gold, platinum, palladium, alloys of these metals or stainless steel. The formation of the recess on the silicon wafer 100 may also be carried out by a dry etch process, or carried out on other substrate materials such as PMMA or photoresist materials and techniques such as laser processing or photo imaging/developing. A compression molding method may further be used to form the recess with the inclined sidewalls. The present invention first preferred embodiment therefore is not limited to a semiconductor formation process. Various other inclined surfaces of the micro-needle may also be formed, such as those shown as a single inclined surface in Figure 6A, double inclined surfaces shown in Figure 7A, or other shapes of the inclined surfaces shown in Figures 6B and 6C.

00031 The density of the micro-needle array formed may be controlled during the lithographic process for defining the wet etched area. By controlling the length and the width of the wet etch area, and by the distance between the wet etch area and by the distance between the wet etch area. Figures 2A-2F illustrates fabrication process steps for a present invention second preferred

embodiment. Figure 2A is similar to that shown in Figure 1A wherein protective layers 202 covers a silicon substrate 200. In the second step of the process, shown in Figure 2B, the wet etch areas 210,220 are defined by a lithographic method with various internal distances A1 and A2. The density of the micro-needle array may further be controlled by defining different distances B1, B2 in between the wet etch areas 210,220 and 230 as shown in Figure 2B. The resulting micro-needle array is shown in Figure 2F. The other processing steps, shown in Figures 2C, 2D and 2E are similar to that described in Figures 1C, 1D and 1E.

00032 The above described processes may further be used for making other micro-needles with other materials by using the metal micro-needles as a mold. This is shown in Figures 3A-3C in a third preferred embodiment of the present invention fabrication method. In this embodiment, a mold release layer 320 such as teflon is first deposited on top of the silicon wafer 300 and in the metal micro-needle 310. The silicon wafer 300 and the metal micro-needle 310 are then heated, followed by pressing a thermoplastic film 330 of polymeric nature uniformly under pneumatic pressure on the metal micro-needle 310. After the thermoplastic thin film 320 conforms to the shape of the metal micro-needle 310, micro-needle 340 can be

demolded after cooled. Other micro-needle arrays formed by various materials can thus be made by using the metal micro-needle as a mold by techniques such as micro injection molding, micro thermal compression molding or transfer molding. The demolding technique can be facilitated by heating, cooling, surface coating, or solvent demolding.

00033 The present invention micro-needle array may further be fabricated by imaging and molding processes. This is shown in Figures 4A-4H in a fourth preferred embodiment for the present invention. As shown in Figure 4A, on top of a silicon wafer 401 is first deposited an etch protective layer 402. A photoresist layer is then deposited and imaged to define areas to be etched, shown in Figure 4B. The etch protective layer 402 is then etched to obtain a wet etch region 403. In the next step of the process, shown in Figure 4C, an anisotropic etching (wet etching) process is carried out on the silicon wafer 401 to obtain a recess 404 that has inclined sidewalls. An anti-reflective coating layer such as a black photoresist layer 405 is then coated, as shown in Figure 4D, followed by the coating of a sacrificial layer such as gold or a mold release layer such as teflon or silicon rubber (PDMS) coating 406. A photoresist layer 407 is then deposited on top of the

structure, as shown in Figure 4E. A first imaging process is carried out to obtain a first exposed area 408. A second imaging process is then carried out, as shown in Figure 4F, to obtain the shape of the micro-needle in a second exposed area 409. The sacrificial layer 406 is then removed, as shown in Figure 4G. The structure may also be demolded directly to obtain a bottom layer 410 is developed with inclined sidewalls. In the final step shown in Figure 4H, the bottom layer 410 is developed to obtain the micro-needle array 420.

00034 In the process discussed above, the major purpose of the anti-reflective coating layer 405 is to prevent any over-exposure of the photoresist layer due to the different exposure depth. The sequence for depositing the anti-reflective layer 405 and the sacrificial layer 406 (or the mold release layer) may be reversed. It is also possible to first demold and then carry out the imaging/developing step.

00035 In still another preferred embodiment of the present invention, more than one layer of a photoresist material may be used to change the internal passageway in the micro-needle, or to merge various internal passageways into a single, large passageway

for taking blood samples or for delivering fluid. This is illustrated in Figures 5A-5G in a fifth preferred embodiment of the present invention fabrication method. In the first step of the process, shown in Figure 5A, a recess 504 with inclined sidewalls is first etched on a silicon wafer 501 covered with a protective layer 502. An anti-reflective layer 505, a sacrificial layer (or mold release layer) 506 are then sequentially deposited. As shown in Figure 5B, a first photoresist layer 507 is coated for carrying out a first imaging/exposure to obtain a first exposure zone 508. A second exposure is then carried out, as shown in Figure 5C. An anti-reflective coating layer 509, a second photoresist layer 510 are then coated and a third exposure process is carried out. This is shown in Figure 5D. Another layer of anti-reflective coating 511, and a second photoresist layer 512 are then sequentially deposited and a fourth exposure process is carried out, as shown in Figure 5E. The sacrificial layer 505 is then removed, or the structure is directly demolded, as shown in Figure 5F to obtain a bottom structure 520 that has inclined surfaces. The bottom structure is then developed to obtain the micro-needle array 530, as shown in Figure 5G.

00036 In the fifth preferred embodiment, the deposition process for the anti-reflective coating layer and for the sacrificial layer (or the mold release layer) may be reversed in sequence. For different structures or configurations, one of the layers also may not be necessary. The second exposure process may further be saved, despite the fact that a stronger bottom structure can be obtained when the second exposure process is used. The photoresist layer may be selected from either a positive photoresist or a negative photoresist. More than one layer of photoresist layer may also be used to form internal passageways of various sizes, i.e., the internal passageway 5A, 5B. The internal passageway may also be connected into an interconnecting network, shown as passageway 5C or a storage region as shown in Figure 5G.

00037 The above-described process can also be used to form micro-needles that have various inclined surface structures at the needle tip. For instance, a single inclined surface is shown in Figure 6A, double inclined surfaces are shown in Figure 7A, other types of inclined surfaces are shown in Figures 6B and 6C.

00038 Figures 8A-8G illustrates a sixth preferred embodiment of the present invention fabrication process. For instance, Figure 8A illustrates that a protective layer 602 is first deposited on top of the silicon wafer 601. A wet etch area 603 is then defined, shown in Figure 8B. The silicon wafer 601 is then etched to obtain a recess 604 equipped with inclined sidewalls. This is shown in Figure 8C. A sacrificial layer 605 or a mold release layer is then deposited, as shown in Figure 8D. Shown in Figures 8E-8G, a plastic material 606 is used to thermal pressure forming a bottom structure 607 equipped with inclined surfaces. The sacrificial layer 605 is then removed, or demolded. A micro-processing technique is then used to define the internal passageways 6a and 6b, as shown in Figure 8H forming the micro-needle array 610. The plastic material utilized may be a thermoset material or a thermoplastic material. The micro-processing technique utilized may be laser processing or etching. The bottom structure 607 may also be formed by an injection molding process.

00039 While the present invention has been described in an illustrative manner, it should be understood that the terminology used is intended to be in a nature of words of description rather than of limitation.

00040 Furthermore, while the present invention has been described in terms of one preferred and five alternate embodiments, it is to be appreciated that those skilled in the art will readily apply these teachings to other possible variations of the inventions.

00041 The embodiment of the invention in which an exclusive property or privilege is claimed are defined as follows.